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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,855	09/14/2005	Hidechika Okada	3348/1	7847

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,855	OKADA ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April, and 04 August, 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11* is/are rejected.

7)☒ Claim(s) *11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04/07/08; 08/04/08* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/04/2005; 05/26/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communications filed 07 April, 2008, and 04 August, 2008. Claims 1-7 have been canceled without prejudice or disclaimer and new claims 8-11 have been introduced.

37 C.F.R. § 1.98

The information disclosure statements filed 04 April, 2005, and 26 May, 2005, have been placed in the application file and the information referred to therein has been considered.

Drawings

The drawings are objected to because they are illegible (see Figures 1-5) and fail to include the appropriate sequence identifiers (see Figure 5). Corrected drawing sheets in compliance with 37 C.F.R. § 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application

must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 C.F.R. § 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

37 C.F.R. § 1.821-1.825

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2) (e.g., see pages 23-25 and 28 of the specification). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825 for the reason(s) previously set forth in the last Office action. Applicants are reminded that sequences appearing in the **specification (e.g., see Tables 1 and 2)** and/or **drawings (e.g., see Figure 5) must** be identified by a sequence identifier (SEQ ID NO.:) in accordance with 37 C.F.R. § 1.821(d). **Applicant must provide appropriate amendments to the specification and/or drawings inserting the required sequence identifiers**. Extensive amendments may necessitate the submission of a substitute specification. The specification is objected to because it fails to meet the requirements set forth *supra*. Applicants' response failed to adequately address this point.

Specification

The specification is objected to because Table 2 is illegible. Appropriate correction is required. Extensive amendments may necessitate the submission of a substitute specification. A substitute specification must not contain new

matter. The substitute specification must be submitted with markings showing all the changes relative to the immediate prior version of the specification of record. The text of any added subject matter must be shown by underlining the added text. The text of any deleted matter must be shown by strikethrough except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strikethrough cannot be easily perceived. An accompanying clean version (without markings) and a statement that the substitute specification contains no new matter must also be supplied. Numbering the paragraphs of the specification of record is not considered a change that must be shown.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The previous rejection of claims 1-7 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is moot in view of applicants' response canceling the claims.

Claims 8-11 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point

out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. First, claim 8 references a Mab that specifically recognizes HIV-infected cells "and including apoptosis" of the infected cells is vague and indefinite. The salient characteristics of the claimed composition are not readily manifest. Applicants should clearly and unambiguously identify the functional characteristics of the claimed antibody (i.e., A monoclonal antibody that binds specifically to HIV-1-infected cells and is capable of **inducing** apoptosis in said cells upon binding...). Second, the reference to a "cell strain with an accession No. FERM BP-8378" is confusing. It appears the claims are actually referencing a hybridoma that produces Mab 2G9. Appropriate correction is required (i.e., wherein said Mab 2G9 is produced from the hybridoma cell line having accession No. FERM BP-8378...). Applicants' response failed to correct these deficiencies.

37 C.F.R. § 1.75(c), Improper Dependent Claim

Claim 11 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 11 simply references a human IgM Mab that is produced by the cell line FERM BP-8378. This is the same cell

line recited in claim 8. Thus, it is not readily manifest how this limitation is further limiting.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Biological Deposit Requirement

The previous rejection of claims 4-7 under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure for the claimed invention, is moot in view of applicants' response and the cancellation of these claims.

Written Description

The previous rejection of claims 1, 4, and 5 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is moot in view of applicants' amendment cancelling these claims.

Scope of Enablement

The previous rejection of claims 1, 4, and 5 under 35 U.S.C. § 112, first paragraph, because the specification does not

reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, is moot in view of applicants' amendment cancelling these claims.

Enablement

The previous rejection of claims 2-5 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement, is moot in view of applicants' amendment cancelling these claims.

Claims 9 and 10 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed toward pharmaceutical compositions comprising an IgM monoclonal antibody (Mab) that recognizes HIV-infected cells and is capable of inducing apoptosis in said cells and capable of treating or preventing HIV infection and the onset of AIDS.

The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount

of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

Problems:

1) The disclosure fails to provide adequate guidance pertaining to the immunologic/pharmacologic properties of the Mab of interest. The disclosure fails to provide any guidance pertaining to the binding specificity, affinity, avidity, half-life, or circulating titer required to achieve a therapeutic response.

2) The disclosure fails to demonstrate if the antibody is capable of binding to both HIV-1- and -2-infected cells. The only examples provided in the specification were directed toward HIV-1-infected cell lines. However, the term HIV encompasses both HIV-1 and -2. Considering the genotypic/phenotypic heterogeneity between the two viruses, directed extrapolations concerning antibody binding cannot be made between the two viruses.1

3) The state-of-the-art as it pertains to the utilization of immunotherapeutics to treat or prevent HIV infectin is quite unpredictable. Several factors have contributed to the failure of immunotherapeutics including low binding affinity, rapid clearance rates, the quasispecies nature of HIV infection which

1 It has been well-documented that HIV-1 and -2 only display ~35-38% genetic relatedness, depending upon the isolate.

leads to rapid immune escape and avoidance, the large quantities of virus produced on a daily basis, and the ability of the virus to reside in immunoprivileged sites. The therapeutic effectiveness of the claimed Mab is also predicated upon its ability to induce apoptosis in HIV-infected cells. However, the claimed Mab only induce apoptosis in ~20% of the cell population examined. This means that ~80% of the cell population is still infected and capable of producing virus. Thus, it does not appear that this would have any meaningful clinical effect.

4) The disclosure fails to provide any working embodiments. The only representative examples disclosed in the specification were directed toward in vitro tissue culture studies which are clearly not predictive of in vivo clinical efficacy. Moreover, no data was provided from a suitable animal model or preliminary clinical trials.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation to practice the claimed invention.

Action Is Final, Necessitated by Amendment

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory

period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system,

see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin/

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

10 November, 2008